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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS 4	OCT 30	CHEMLIST enhanced with new search and display field
NEWS 5	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 6	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS 7	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS 8	NOV 20	CAS Registry Number crossover limit increased to 300,000 in additional databases
NEWS 9	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 10	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS 11	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS 12	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS 13	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS 14	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 15	DEC 18	CA/CAplus patent kind codes updated
NEWS 16	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 17	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 18	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS 19	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 20	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 21	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 22	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data

NEWS EXPRESS	NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:30:52 ON 19 JAN 2007

=> EGISTRY
EGISTRY IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> FILE REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 13:31:08 ON 19 JAN 2007
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 18 JAN 2007 HIGHEST RN 917867-30-2
DICTIONARY FILE UPDATES: 18 JAN 2007 HIGHEST RN 917867-30-2

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TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> S 235108-14-2/RN
L1 1 235108-14-2/RN

=> S 213319-29-0/RN
L2 1 213319-29-0/RN

=> S 2133250-70-5/RN
L3 0 2133250-70-5/RN

=> S 213250-70-5/RN
L4 1 213250-70-5/RN

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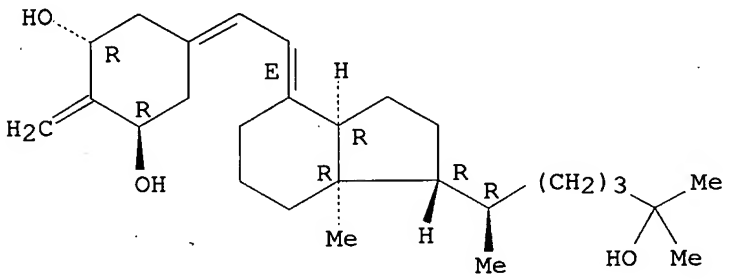
=> D L1 AND L2 AND L4
L2 IS NOT VALID HERE
For an explanation, enter "HELP DISPLAY".

=> D L1

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 235108-14-2 REGISTRY
ED Entered STN: 26 Aug 1999
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
(1α,3β,7E,14β)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H44 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> D L2

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 213319-29-0 REGISTRY
ED Entered STN: 28 Oct 1998
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
(1α,3β,7E)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-1-[(1R)-5-hydroxy-1,5-dimethylhexyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, (1R,3R)-
FS STEREOSEARCH
MF C27 H44 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

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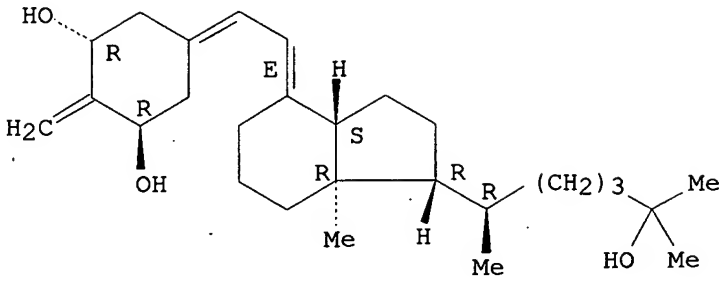


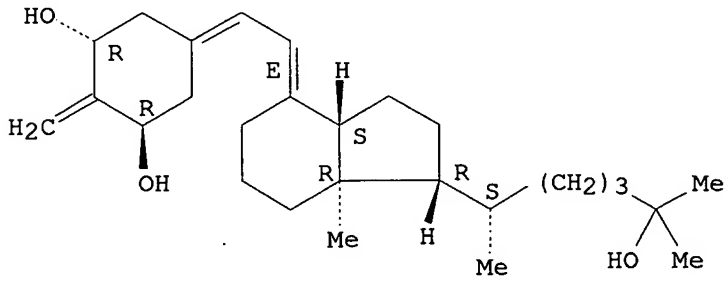
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

29 REFERENCES IN FILE CA (1907 TO DATE)
29 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> D L4

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 213250-70-5 REGISTRY
ED Entered STN: 27 Oct 1998
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-1-[(1S)-5-hydroxy-1,5-dimethylhexyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, (1R,3R)-
CN 2-Methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D3
CN 2MD
FS STEREOSEARCH
MF C27 H44 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, IMSDRUGNEWS, IMSRESEARCH, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

48 REFERENCES IN FILE CA (1907 TO DATE)

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48 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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=> FILE CAPLUS
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     8.10       8.31

FILE 'CAPLUS' ENTERED AT 13:33:54 ON 19 JAN 2007
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FILE LAST UPDATED: 18 Jan 2007  (20070118/ED)

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=> S L1 AND L2 AND L4
             1 L1
            29 L2
            48 L4
L5           0 L1 AND L2 AND L4

=> 1 L1
1 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> S L1
L6           1 L1

=> S L2
L7          29 L2

=> S L4
L8          48 L4

=> S L7 AND L8
L9          27 L7 AND L8

=> S L1 OR  L2 OR  L4 AND CANCER
             1 L1
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            29 L2
            48 L4
        303251 CANCER
L10         34 L1 OR  L2 OR  L4 AND CANCER

=> D L10 1-34 IBIB HITSTR ABS
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L10 ANSWER 1 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:283341 CAPLUS
DOCUMENT NUMBER: 142:310363
TITLE: Preparation of 2-alkylidene-19-nor-vitamin D derivatives for the treatment of hypocalcemic tetany or hypoparathyroidism
INVENTOR(S): Miller, Jeffrey Wells; Nduaka, Chudi Ike
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027928	A1	20050331	WO 2004-IB2910	20040906
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005101578	A1	20050512	US 2004-943562	20040916
PRIORITY APPLN. INFO.:			US 2003-504022P	P 20030919

IT 213319-29-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-alkylidene-19-nor-vitamin D derivs. for treatment of hypocalcemic tetany or hypoparathyroidism)

RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

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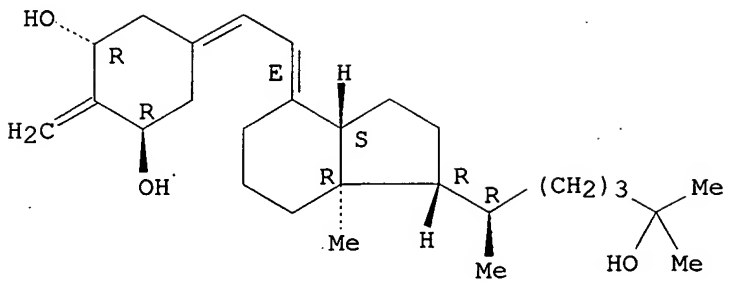


AB The present invention relates to methods of treating hypocalcemic tetany or hypoparathyroidism, the methods comprising administering to a patient in need thereof a 2-alkylidene-1 9-nor-vitamin D derivative Particularly, the present invention relates to methods of treating hypocalcemic tetany or hypoparathyroidism, the methods comprising administering to a patient in need thereof a therapeutically effective amount of 2-methylene-19-nor-20(S)-1a,25-dihydroxyvitamin D3.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

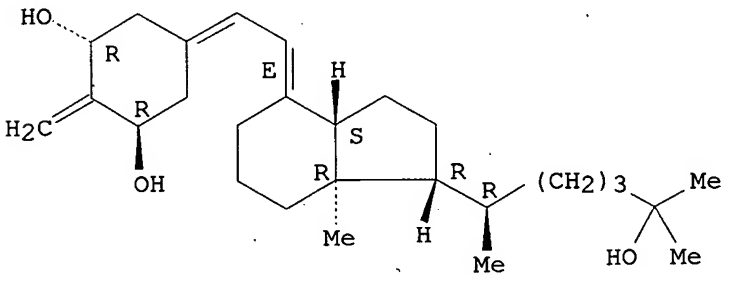
L10 ANSWER 2 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:283340 CAPLUS
DOCUMENT NUMBER: 142:341912
TITLE: Pharmaceutical compositions and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivatives and an estrogen agonist/antagonist
INVENTOR(S): Lee, Andrew George
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027924	A1	20050331	WO 2004-IB2900	20040906
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004273658	A1	20050331	AU 2004-273658	20040906
CA 2539361	A1	20050331	CA 2004-2539361	20040906
EP 1667692	A1	20060614	EP 2004-769299	20040906
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1852720	A	20061025	CN 2004-80026832	20040906

BR 2004014448	A	20061114	BR 2004-14448		20040906
US 2005070512	A1	20050331	US 2004-943568		20040916
NO 2006001702	A	20060619	NO 2006-1702		20060418
PRIORITY APPLN. INFO.:			US 2003-504521P	P	20030919
			WO 2004-IB2900	W	20040906

IT 213319-29-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical combinations of 2-alkylidene-19-nor-vitamin D derivs. and an estrogen agonist/antagonist)
RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB The present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof a combination of a 2-alkylidene-19-nor-vitamin D derivative and an estrogen agonist/antagonist or a pharmaceutically acceptable salt or prodrug thereof. Particularly, the present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-Ia,25-dihydroxyvitamin D3 and (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydronaphthalene-2-ol, or a pharmaceutically acceptable salt or prodrug thereof.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2005:283339 CAPLUS
DOCUMENT NUMBER:	142:310362
TITLE:	Preparation of 2-alkylidene-19-nor-vitamin D derivatives for the treatment of rickets or vitamin D deficiency
INVENTOR(S):	Miller, Jeffrey Wells; Nduaka, Chudi Ike
PATENT ASSIGNEE(S):	Pfizer Products Inc., USA
SOURCE:	PCT Int. Appl., 42 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

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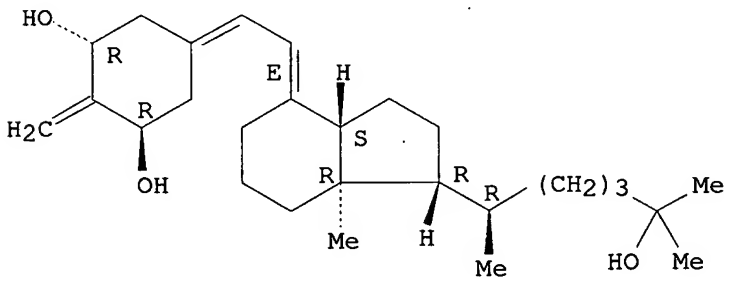
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027920	A1	20050331	WO 2004-IB2925	20040906
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005101577	A1	20050512	US 2004-942382	20040916
PRIORITY APPLN. INFO.:			US 2003-503811P	P 20030919

IT 213319-29-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-alkylidene-19-nor-vitamin D derivs. for the treatment of rickets or vitamin D deficiency)
RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB The present invention relates to methods of treating vitamin D deficiency, particularly rickets, the methods comprising administering to a patient in need thereof a 2-alkylidene-19-nor-vitamin D derivative Particularly, the present invention relates to methods of treating vitamin D deficiency with 2-methylene-19-nor-20(S)-1a,25-dihydroxyvitamin D3.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:259681 CAPLUS
DOCUMENT NUMBER: 142:317006
TITLE: Pharmaceutical compositions and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivatives and a growth hormone secretagogue
INVENTOR(S): Lee, Andrew G.
PATENT ASSIGNEE(S): Pfizer Inc, USA
SOURCE: U.S. Pat. Appl. Publ., 23 pp.

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CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005065180	A1	20050324	US 2004-942376	20040916
WO 2005027913	A1	20050331	WO 2004-IB2899	20040906

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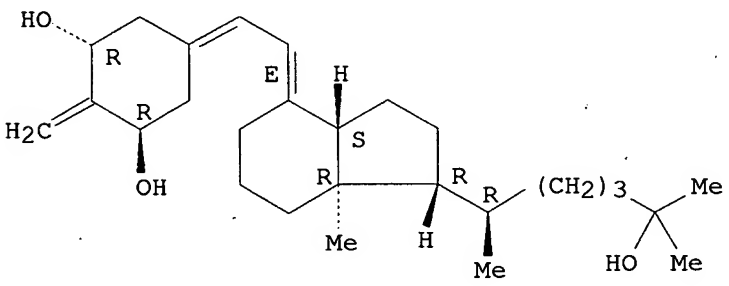
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-504001P P 20030919

IT 213319-29-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation 2-methylene-19-norvitamin D derivs. for use in compns. with a growth hormone secretagogue)

RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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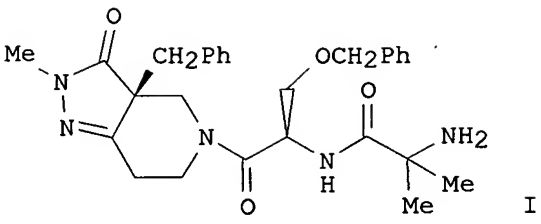

I

AB The present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof a combination of a 2-alkylidene-19-nor-vitamin D derivative and a growth hormone secretagogue or a pharmaceutically acceptable salt or prodrug thereof. Particularly, the present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D3 and a growth hormone secretagogue (e.g. I) or a pharmaceutically acceptable salt or prodrug thereof.

L10 ANSWER 5 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:259665 CAPLUS
DOCUMENT NUMBER: 142:310360
TITLE: Preparation of 2-alkylidene-19-nor-vitamin D derivatives for the treatment of anorexia or low bone mass in females exhibiting aggressive athletic behavior
INVENTOR(S): Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005065134	A1	20050324	US 2004-944368	20040916
WO 2005027925	A1	20050331	WO 2004-IB2904	20040906

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-504510P P 20030919
OTHER SOURCE(S): CASREACT 142:310360
IT 213319-29-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

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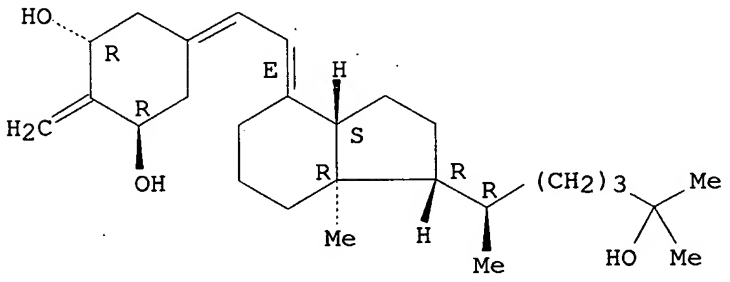
(Uses)
(preparation of 2-alkylidene-19-nor-vitamin D derivs. for treatment of anorexia or low bone mass in females exhibiting aggressive athletic behavior)

RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB The present invention relates to methods of treating anorexia or low bone mass in females exhibiting aggressive athletic behavior, the methods comprising administering to a patient in need thereof a 2-alkylidene-19-nor-vitamin D derivative Particularly, the present invention relates to methods of treating anorexia or low bone mass in females exhibiting aggressive athletic behavior, the methods comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-1α,25-dihydroxy-vitamin D3.

L10 ANSWER 6 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2005:259664 CAPLUS
DOCUMENT NUMBER:	142:317005
TITLE:	Pharmaceutical compositions and methods comprising combinations of 2-alkylidene-19-nor-vitamin d derivatives and an ep2 or ep4 selective agonist
INVENTOR(S):	Lee, Andrew G.; Thompson, David D.
PATENT ASSIGNEE(S):	Pfizer Inc., USA
SOURCE:	U.S. Pat. Appl. Publ., 49 pp. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005065133	A1	20050324	US 2004-944119	20040916
WO 2005027931	A1	20050331	WO 2004-IB2949	20040906

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,

QAZI

AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

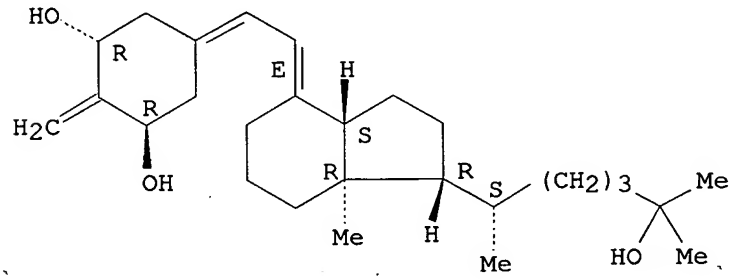
PRIORITY APPLN. INFO.: US 2003-503798P P 20030919

IT 213250-70-5P 213319-29-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compns. and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivs. and aromatase inhibitors)

RN 213250-70-5 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

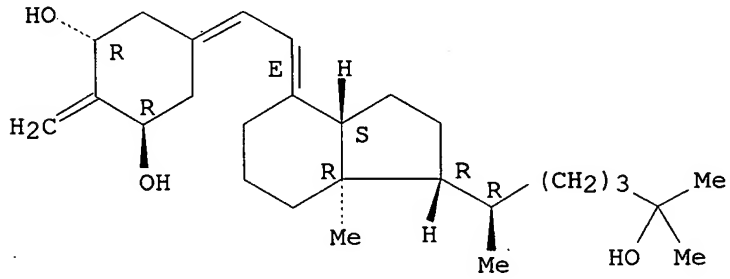
Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB The present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof a combination of a 2-alkylidene-19-nor-vitamin D derivative and an EP2 or EP4 selective agonist or a pharmaceutically acceptable salt or prodrug thereof. Particularly, the present invention relates to pharmaceutical compns. and methods comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D3 and an EP2 or EP4 selective agonist or a pharmaceutically acceptable salt or prodrug thereof.

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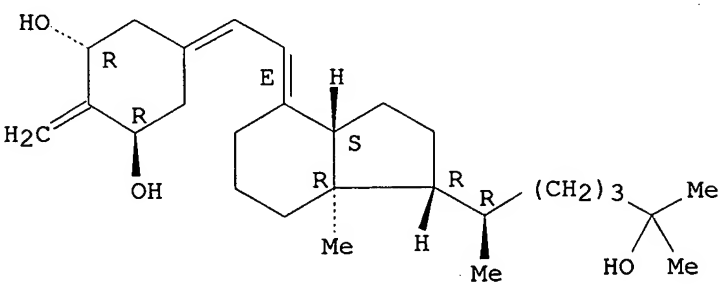
L10 ANSWER 7 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:259663 CAPLUS
DOCUMENT NUMBER: 142:310359
TITLE: Preparation of 2-alkylidene-19-nor-vitamin D derivatives for the treatment or prevention of a second hip fracture
INVENTOR(S): Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005065132	A1	20050324	US 2004-944065	20040916
WO 2005027919	A1	20050331	WO 2004-IB2914	20040906

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-504004P P 20030919
OTHER SOURCE(S): CASREACT 142:310359
IT 213319-29-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-alkylidene-19-nor-vitamin D derivs. for treatment or prevention of a second hip fracture)
RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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AB The present invention relates to methods of treating or preventing a second hip fracture, the methods comprising administering to a patient in need thereof a 2-alkylidene-19-nor-vitamin D derivative Particularly, the present invention relates to methods of treating or preventing a second hip fracture, the methods comprising administering to a patient in need thereof a therapeutically effective amount of 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D 3.

L10 ANSWER 8 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:259662 CAPLUS
DOCUMENT NUMBER: 142:310358
TITLE: Preparation of 2-alkylidene-19-nor-vitamin D derivatives for enhancement of peak bone mass in adolescence
INVENTOR(S): Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005065131	A1	20050324	US 2004-944063	20040916
WO 2005027927	A1	20050331	WO 2004-IB2906	20040906

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-504511P P 20030919
OTHER SOURCE(S): CASREACT 142:310358
IT 213319-29-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-alkylidene-19-nor-vitamin D derivs. for enhancement of peak bone mass in adolescence)
RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

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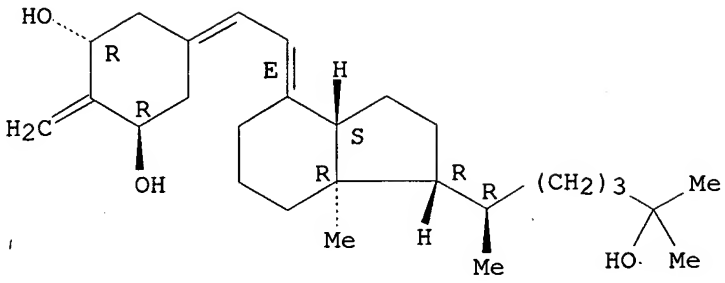

AB The present invention relates to methods of enhancing peak bone mass in adolescence, the methods comprising administering to a patient in need thereof a 2-alkylidene-19-nor-vitamin D derivative Particularly, the present invention relates to methods of enhancing peak bone mass in adolescence, the methods comprising administering to a patient in need thereof a therapeutically effective amount of 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D3.

L10 ANSWER 9 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:259661 CAPLUS
DOCUMENT NUMBER: 142:336520
TITLE: Preparation, pharmaceutical compositions, and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivatives and a cyclooxgenase-2 inhibitor
INVENTOR(S): Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005065130	A1	20050324	US 2004-943561	20040916
WO 2005027918	A1	20050331	WO 2004-IB2913	20040906

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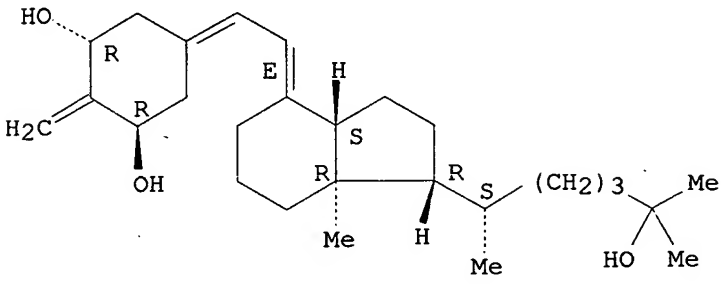
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-504003P P 20030919
IT 213250-70-5P 213319-29-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of and pharmaceutical compns. and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivs. and aromatase

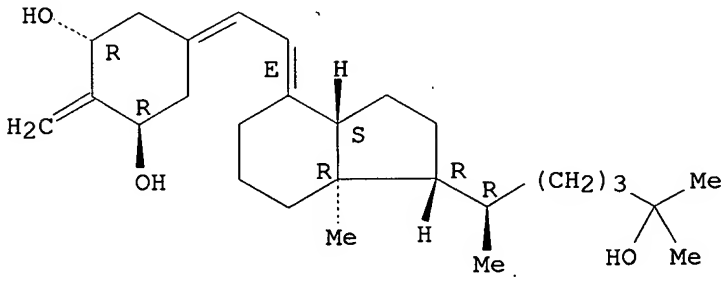
inhibitors)
RN 213250-70-5 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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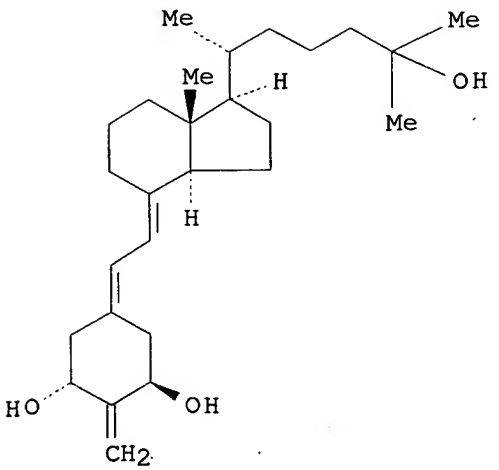

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AB The invention relates to pharmaceutical compns., and methods of treatment comprising administering to a patient in need of a combination of a 2-alkylidene-19-nor-vitamin D derivative and a cyclooxgenase-2 inhibitor, or a pharmaceutically acceptable salt or prodrug thereof. Particularly, the invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need of 2-methylene-19-nor-20(S)-10,25-dihydroxyvitamin D3 and a cyclooxgenase-2 inhibitor, or a pharmaceutically acceptable salt or prodrug thereof. Thus, 1α,25-dihydroxy-2-methylene-19-norvitamin D3 (I) was prepared in 11 steps from (-)-quinic acid. and (20S)-1α,25-dihydroxy-2-methylene-19-norvitamine D3 was prepared from (20S)-25-[(triethylsilyl)oxy]-des-A,B-cholestan-8-one in 4 steps.

L10 ANSWER 10 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:259660 CAPLUS
DOCUMENT NUMBER: 142:310357
TITLE: Preparation of 2-alkylidene-19-nor-vitamin D derivatives for the treatment of frailty, muscle damage or sarcopenia
INVENTOR(S): Lee, Andrew G.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005065129	A1	20050324	US 2004-943553	20040916
AU 2004273659	A1	20050331	AU 2004-273659	20040906
CA 2538993	A1	20050331	CA 2004-2538993	20040906
WO 2005027914	A1	20050331	WO 2004-IB2901	20040906

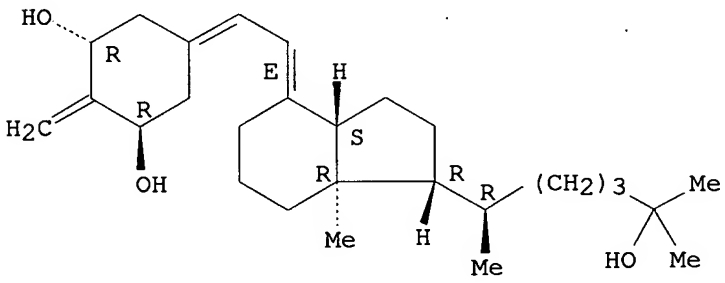
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

EP 1667688	A1	20060614	EP 2004-769300		20040906
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK					
CN 1852718	A	20061025	CN 2004-80027153		20040906
BR 2004014564	A	20061107	BR 2004-14564		20040906
NO 2006001704	A	20060619	NO 2006-1704		20060418
PRIORITY APPLN. INFO.:			US 2003-504509P	P	20030919
			WO 2004-IB2901	W	20040906

IT 213319-29-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-alkylidene-19-nor-vitamin D derivs. for the treatment of frailty, muscle damage or sarcopenia)
RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB The present invention relates to methods of treating frailty, muscle damage or sarcopenia, the methods comprising administering to a patient in need thereof a 2-alkylidene-19-nor-vitamin D derivative Particularly, the present invention relates to methods of treating frailty, muscle damage or sarcopenia, the methods comprising administering to a patient in need thereof a therapeutically effective amount of 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D3.

L10 ANSWER 11 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:259659 CAPLUS
DOCUMENT NUMBER: 142:310356
TITLE: Preparation of 2-alkylidene-19-nor-vitamin D derivatives for the treatment of hypogonadism or andropause
INVENTOR(S): Campagnari, Judith L.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO

QAZI

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005065128	A1	20050324	US 2004-943059	20040916
WO 2005027922	A1	20050331	WO 2004-IB2937	20040906

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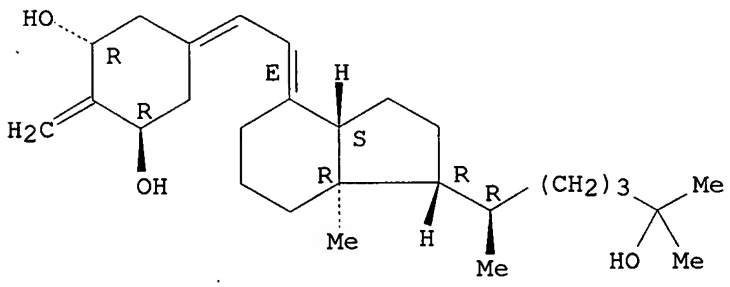
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-503810P P 20030919
OTHER SOURCE(S): MARPAT 142:310356
IT 213319-29-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-alkylidene-19-nor-vitamin D derivs. for treatment of hypogonadism or andropause)
RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB The present invention relates to methods of treating hypogonadism or andropause, the methods comprising administering to a patient in need thereof a 2-alkylidene-19-nor-vitamin D derivative Particularly, the present invention relates to methods of treating hypogonadism or andropause, the methods comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D 3.

L10 ANSWER 12 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:259658 CAPLUS
DOCUMENT NUMBER: 142:310355
TITLE: Preparation of 2-alkylidene-19-nor-vitamin D

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derivatives for the treatment of osteosarcoma

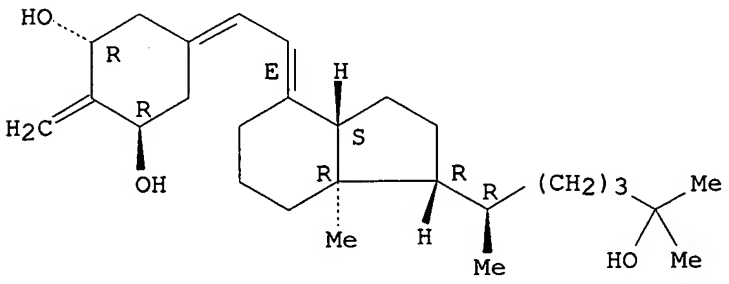
INVENTOR(S): Campagnari, Judith L.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005065127	A1	20050324	US 2004-942704	20040916
WO 2005027930	A1	20050331	WO 2004-IB2918	20040906

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-504021P P 20030919
OTHER SOURCE(S): MARPAT 142:310355
IT 213319-29-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-alkylidene-19-nor-vitamin D derivs. for treatment of osteosarcoma)
RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB The present invention relates to methods of treating osteosarcoma, the methods comprising administering to a patient in need thereof a 2-alkylidene-19-nor-vitamin D derivative Particularly, the present invention relates to methods of treating osteosarcoma, the methods comprising administering to a patient in need thereof a therapeutically effective amount of 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D 3.

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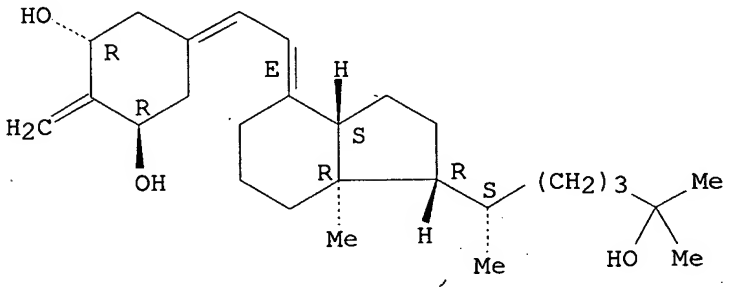
L10 ANSWER 13 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:259657 CAPLUS
DOCUMENT NUMBER: 142:317004
TITLE: Pharmaceutical compositions and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivatives and aromatase inhibitors
INVENTOR(S): Lee, Andrew G.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 19 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005065126	A1	20050324	US 2004-942613	20040916
WO 2005027916	A1	20050331	WO 2004-IB2903	20040906

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-504005P P 20030919
IT 213250-70-5P 213319-29-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compns. and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivs. and aromatase inhibitors)
RN 213250-70-5 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 CAPLUS

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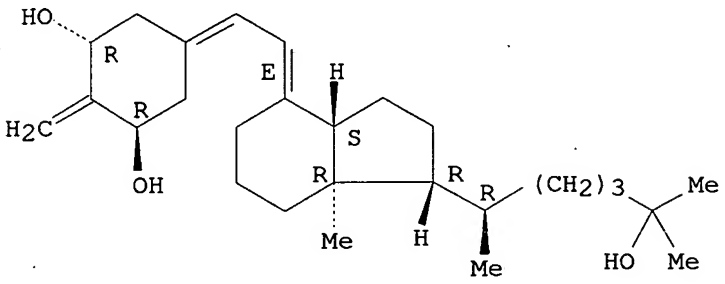
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB The present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof a combination of a 2-alkylidene-19-nor-vitamin D derivative and an aromatase inhibitor. Particularly, the present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D3 and an aromatase inhibitor.

L10 ANSWER 14 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:259656 CAPLUS
DOCUMENT NUMBER: 142:310354
TITLE: Preparation of 2-alkylidene-19-nor-vitamin D derivatives for the treatment of osteopenia or male osteoporosis
INVENTOR(S): Campagnari, Judith L.; Lee, Andrew G.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005065125	A1	20050324	US 2004-942377	20040916
AU 2004273667	A1	20050331	AU 2004-273667	20040906
CA 2539358	A1	20050331	CA 2004-2539358	20040906
WO 2005027917	A1	20050331	WO 2004-IB2912	20040906

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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EP 1667690	A1	20060614	EP 2004-769311		20040906
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK					
CN 1852717	A	20061025	CN 2004-80026946		20040906
BR 2004014465	A	20061114	BR 2004-14465		20040906
NO 2006000655	A	20060616	NO 2006-655		20060209
PRIORITY APPLN. INFO.:			US 2003-504508P	P	20030919
			WO 2004-IB2912	W	20040906

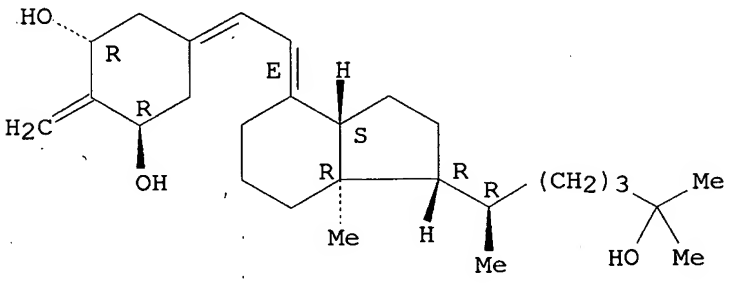
OTHER SOURCE(S): MARPAT 142:310354

IT 213319-29-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-alkylidene-19-nor-vitamin D derivs. for treatment of osteopenia or male osteoporosis)

RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB The present invention relates to methods of treating osteopenia or male osteoporosis, the methods comprising administering to a patient in need thereof a 2-alkylidene-19-nor-vitamin D derivative Particularly, the present invention relates to methods of treating osteopenia or male osteoporosis, the methods comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D 3.

L10 ANSWER 15 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

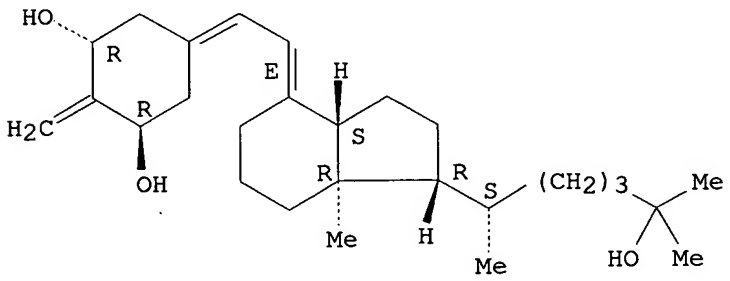
ACCESSION NUMBER:	2005:259654 CAPLUS
DOCUMENT NUMBER:	142:291906
TITLE:	Use of 2-methylene-19-nor-20(s)-1alpha,25-dihydroxyvitamin D3 to increase the life expectancy of human beings
INVENTOR(S):	DeLuca, Hector F.; Plum, Lori A.; Clagette-Dame, Margaret
PATENT ASSIGNEE(S):	USA
SOURCE:	U.S. Pat. Appl. Publ., 5 pp. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2005065123	A1	20050324	US 2003-669990	20030924
AU 2004280176	A1	20050421	AU 2004-280176	20040728
CA 2540051	A1	20050421	CA 2004-2540051	20040728
WO 2005034959	A1	20050421	WO 2004-US24482	20040728
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1663251	A1	20060607	EP 2004-757375	20040728
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2006241090	A1	20061026	US 2006-472125	20060621
PRIORITY APPLN. INFO.:			US 2003-669990 A	20030924
			WO 2004-US24482 W	20040728

IT 213250-70-5, 2-Methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for increasing the life expectancy of human beings)
RN 213250-70-5 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB The invention provides pharmaceutical uses for 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D3. Administration of this compound increases the life expectancy of human beings, especially elderly human beings. In particular, it increases the survival rate of females lacking estrogen, especially post-menopausal females, and reduces mortality resulting from spontaneous development of malignant tumors in both males and females.

L10 ANSWER 16 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:259653 CAPLUS
DOCUMENT NUMBER: 142:317003
TITLE: Pharmaceutical compositions and methods comprising combinations of 2-alkylidene-19-nor-vitamin D

derivatives and a bisphosphonate

INVENTOR(S): Lee, Andrew G.
PATENT ASSIGNEE(S): Pfizer Inc, USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005065117	A1	20050324	US 2004-942426	20040916
AU 2004273672	A1	20050331	AU 2004-273672	20040906
CA 2539359	A1	20050331	CA 2004-2539359	20040906
WO 2005027921	A1	20050331	WO 2004-IB2935	20040906
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1667691	A1	20060614	EP 2004-769333	20040906
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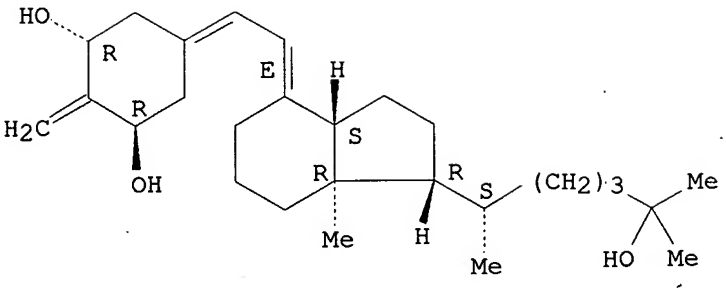
CN 1852719	A	20061025	CN 2004-80027165	20040906
BR 2004014565	A	20061107	BR 2004-14565	20040906
NO 2006001245	A	20060531	NO 2006-1245	20060317

PRIORITY APPLN. INFO.: US 2003-504008P P 20030919
WO 2004-IB2935 W 20040906

IT 213250-70-5P 213319-29-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compns. and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivs. and aromatase inhibitors)
RN 213250-70-5 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

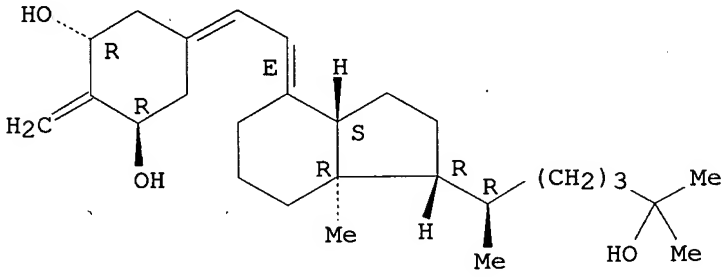
Absolute stereochemistry.
Double bond geometry as shown.

QAZI



RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB The present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof a combination of a 2-alkylidene-19-nor-vitamin D derivative and a bisphosphonate. Particularly, the present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D3 and a bisphosphonate.

L10 ANSWER 17 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:259643 CAPLUS
DOCUMENT NUMBER: 142:317002
TITLE: Pharmaceutical compositions and methods comprising combinations of 2-alkylidene-19-nor-vitamin d derivatives and parathyroid hormone
INVENTOR(S): Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 19 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005065088	A1	20050324	US 2004-946585	20040916

AU 2004273660	A1	20050331	AU 2004-273660	20040906
CA 2539357	A1	20050331	CA 2004-2539357	20040906
WO 2005027915	A1	20050331	WO 2004-IB2902	20040906

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1667689	A1	20060614	EP 2004-769301	20040906

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

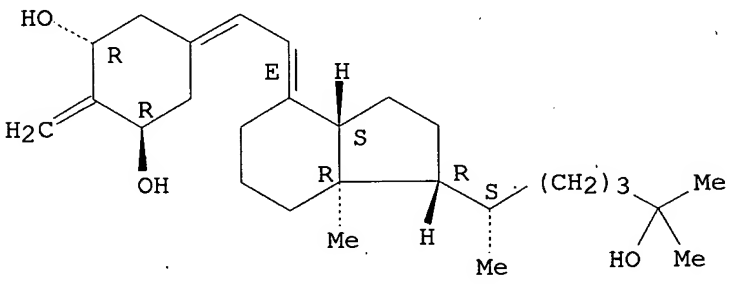
CN 1852716	A	20061025	CN 2004-80026848	20040906
BR 2004014518	A	20061107	BR 2004-14518	20040906
NO 2006001236	A	20060615	NO 2006-1236	20060317
PRIORITY APPLN. INFO.:			US 2003-504503P	P 20030919
			WO 2004-IB2902	W 20040906

OTHER SOURCE(S): CASREACT 142:317002

IT 213250-70-5P 213319-29-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compns. and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivs. and parathyroid hormone)

RN 213250-70-5 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

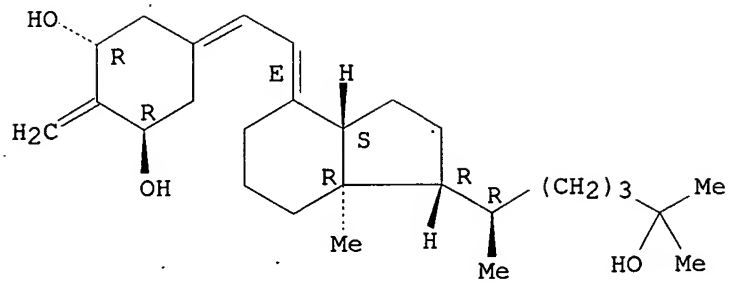
Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

QAZI



AB The present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof a combination of a 2-alkylidene-19-nor-vitamin D derivative and parathyroid hormone or an active fragment or variant thereof. Particularly, the present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D3 and parathyroid hormone or an active fragment or variant thereof.

L10 ANSWER 18 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:259642 CAPLUS
DOCUMENT NUMBER: 142:317001
TITLE: Pharmaceutical compositions and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivatives and a bone morphogenetic protein
INVENTOR(S): Campagnari, Judith L.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 18 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005065087	A1	20050324	US 2004-942725	20040916
WO 2005027926	A1	20050331	WO 2004-IB2905	20040906

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-504161P P 20030919
IT 213250-70-5P 213319-29-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compns. and methods comprising combinations of

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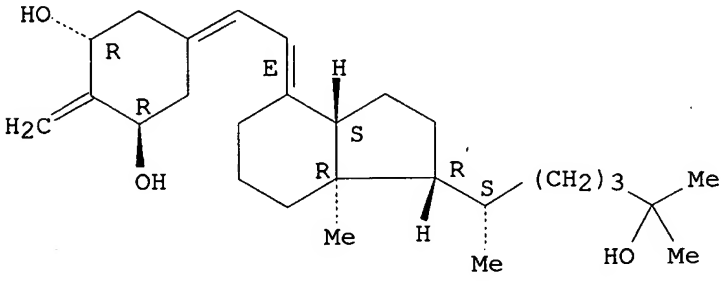
2-alkylidene-19-nor-vitamin D derivs. and bone morphogenetic protein)

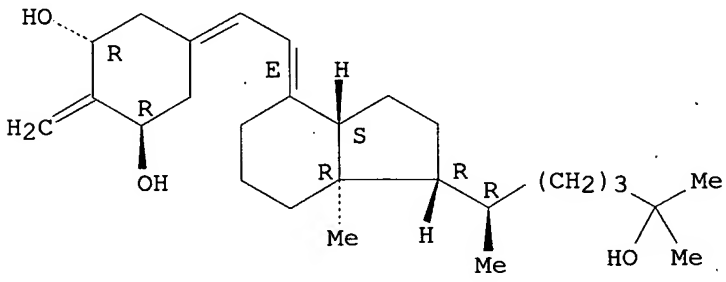
RN 213250-70-5 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB The present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof a combination of a 2-alkylidene-19-nor-vitamin D derivs. and a bone morphogenetic protein or active fragment or variant thereof. Particularly, the present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D 3 and a bone morphogenetic protein or active fragment or variant thereof.

L10 ANSWER 19 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:259356 CAPLUS
DOCUMENT NUMBER: 142:322752
TITLE: Pharmaceutical compositions and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivatives and an estrogen
INVENTOR(S): Keys, Sharon C.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 19 pp.
CODEN: USXXCO

QAZI

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005063992	A1	20050324	US 2004-942384	20040916
WO 2005027929	A1	20050331	WO 2004-IB2911	20040906

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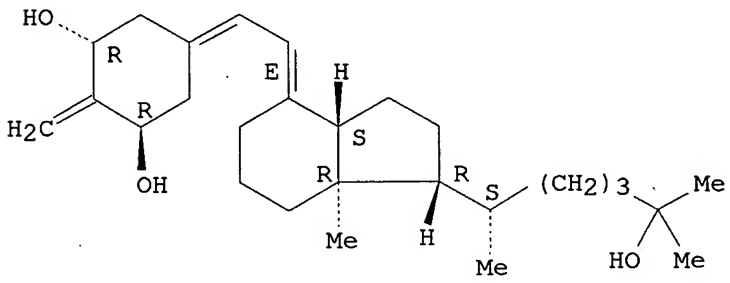
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-504023P P 20030919

IT 213250-70-5P 213319-29-0P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(compns. comprising alkylidene vitamin D derivs. in combination with estrogen for treatment of bone disease, cancer and other diseases)

RN 213250-70-5 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

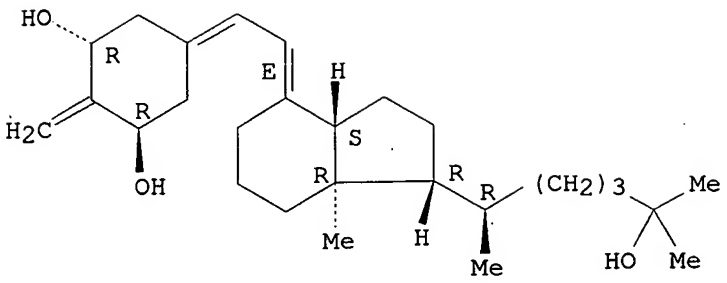
Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

QAZI

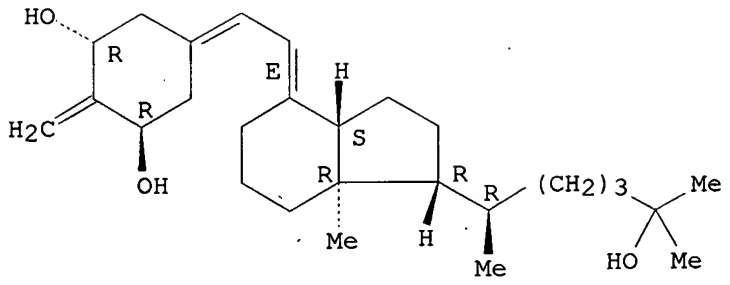


AB The present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof a combination of a 2-alkylidene-19-nor-vitamin D derivative and an estrogen, or a pharmaceutically acceptable salt or prodrug thereof. Particularly, the present invention relates to pharmaceutical compns. and methods of treatment, e.g. osteoporosis, bone fracture, breast cancer, prostate cancer, obesity, osteopenia, etc., comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D3 (I) and an estrogen, or a pharmaceutically acceptable salt or prodrug thereof. For example, I was prepared and tested for biol. activity. I bound well to the porcine intestinal vitamin D receptor. When given at 130 pmol/day, its activity on bone calcium mobilization (serum calcium) was of the order of at least 10 and possible 100 to 1000 times more than that of the native hormone. Also, I was extremely potent in inducing differentiation of HL-60 cells to monocyte, illustrating its potential as anticancer agent.

L10 ANSWER 20 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:522177 CAPLUS
DOCUMENT NUMBER: 141:185224
TITLE: Model of three-dimensional structure of VDR bound with Vitamin D3 analogs substituted at carbon-2
AUTHOR(S): Sicinska, Wanda; Rotkiewicz, Piotr; DeLuca, Hector F.
CORPORATE SOURCE: Department of Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706, USA
SOURCE: Journal of Steroid Biochemistry and Molecular Biology (2004), 89-90(1-5), 107-110
CODEN: JSBBEZ; ISSN: 0960-0760
PUBLISHER: : Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 213319-29-0
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(model of three-dimensional structure of VDR bound with Vitamin D3 analogs substituted at carbon-2)
RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

QAZI



AB All Vitamin D analogs possessing the A ring modified at C-2 and showing calcemic activities nest themselves in the VDR binding pocket, oriented towards Tyr 143. Such topol. resembles the position of the Vitamin D hormone in hVDRmt [Proc. Natl. Acad. Sci. U.S.A. 98 (2001) 5491]. Conversely, inactive 2β-methyl-19-nor-analogs anchor the receptor cavity in a distinguishably different manner, namely by their side chain. Moreover, these inactive vitamins have a different conformation around C(6)-C(7) bond. Topol. of modeled complexes suggests that a Vitamin D analog will be biol. active if its intercyclic 5,7-diene moiety assumes parallel position to tryptophan aromatic rings; such orientation allows for creating π-π interactions. The broad comparison of calcemic activities of the analogs, and their interactions with VDR, revealed that specific hydrophobic contacts are involved in bone calcium mobilization (BCM). These contacts occur between 21-Me group and a few amino acids (V296, L305 and L309), conserved in the nuclear receptor superfamily. In the inactive 2β-methyl-19-nor analogs such contacts do not exist. We speculate that two hydrophobic receptor patches, being in close contact with ligand Me groups, might influence interaction with co-modulators involved in calcium homeostasis.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 21 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:522171 CAPLUS
DOCUMENT NUMBER: 141:185221
TITLE: Therapeutic potential of the 2-alkyl and 2-alkylidene-19-nor-(20S)-modified analogs of 1α,25-dihydroxyvitamin D3
AUTHOR(S): DeLuca, Hector F.
CORPORATE SOURCE: Department of Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706-1544, USA
SOURCE: Journal of Steroid Biochemistry and Molecular Biology (2004), 89-90(1-5), 67-73
CODEN: JSBBEZ; ISSN: 0960-0760
PUBLISHER: : Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 213250-70-5
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of 2-alkyl and 2-alkylidene-19-nor-(20S)-modified analogs of 1α,25-(OH)2D3 on PTH activity/bone mineral mobilization, and their therapeutic potential for diseases where a rise in serum calcium is not desired).
RN 213250-70-5 CAPLUS

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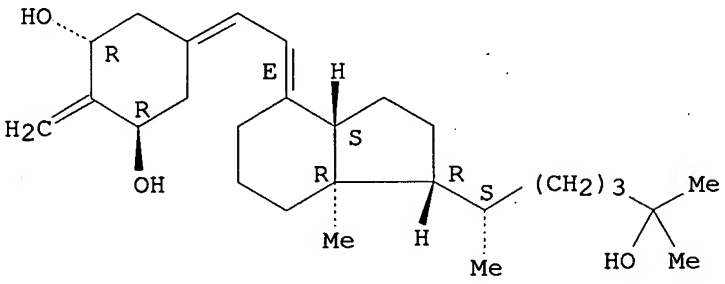
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB Five analogs of 19-nor-1α,25-dihydroxyvitamin D3 are described that show highly selective and potent activities. The 2-methylene-19-nor-(20S)-1α25-dihydroxyvitamin D3 (2MD) and its 2α-Me sister are selectively active on the osteoblast. 2MD is bone anabolic and causes bone formation in vivo and in vitro and is being developed as a therapy for bone loss diseases such as osteoporosis. 2-Methylene-19-nor (20S)-bishomo-1α-hydroxypregnacalciferol (2BMP) has no activity on calcium in vivo while totally suppressing circulating parathyroid hormone. Its homologs, i.e. 2-methylene-19-nor-1α-hydroxy-homopregnacalciferol (2MP) and 2-methylene-19-nor-1α-hydroxypregnacalciferol (2MPC) act similarly but are either less selective (2MP) or not as potent (2MPC). These abbreviated side chain analogs will be developed for diseases where a rise in serum calcium is not desired, as for example, cancer, renal osteodystrophy, psoriasis and autoimmune diseases.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 22 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:220021 CAPLUS
DOCUMENT NUMBER: 140:247113
TITLE: Method of extending the dose range of vitamin D compounds
INVENTOR(S): Deluca, Hector F.; Pike, John W.; Shevde, Nirupama; Plum, Lori A.; Clagett-Dame, Margaret
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 17 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004053813	A1	20040318	US 2002-235244	20020905
CA 2497828	A1	20040318	CA 2003-2497828	20030626
WO 2004022068	A1	20040318	WO 2003-US20517	20030626

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003245748	A1	20040329	AU 2003-245748		20030626
EP 1545549	A1	20050629	EP 2003-739354		20030626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003014006	A	20050809	BR 2003-14006		20030626
CN 1694711	A	20051109	CN 2003-824888		20030626
JP 2006500388	T	20060105	JP 2004-534233		20030626
PRIORITY APPLN. INFO.:			US 2002-235244	A	20020905
			WO 2003-US20517	W	20030626

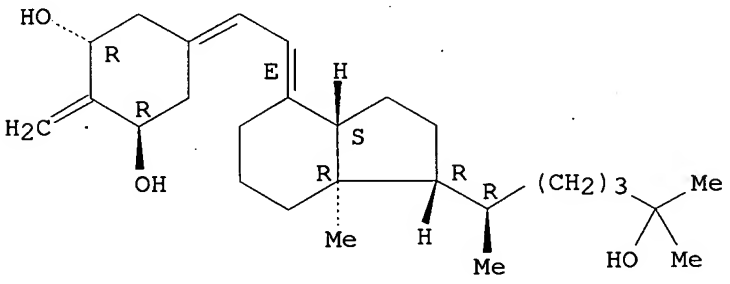
OTHER SOURCE(S): MARPAT 140:247113

IT 213319-29-0
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of extending dose range of vitamin D compds.)

RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB Inhibitors of bone calcium resorption are administered to allow high doses of vitamin D compds. or mimetics (Markush structures are given) to be given with the intent of treating non-calcium related diseases such as cancer, psoriasis, and autoimmune disease without the dangers of calcification of kidney, heart, and aorta. Inhibitors of bone calcium resorption include the bis-phosphonates, OPG or the soluble RANKL receptor known as sRANK, and function to block the availability of calcium from bone thereby preventing hypercalcemia and the resulting calcification of soft tissues. Thus, high doses of 1α,25-dihydroxyvitamin D 3 (1,25-(OH) 2 D 3), its analogs, prodrugs, or mimetics can be utilized with minimal risk to a patient. Specifically, alendronate is shown to block the bone calcium mobilization activity of both 1,25-(OH) 2 D 3 and its very potent analog, 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D 3 .

L10 ANSWER 23 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:647469 CAPLUS

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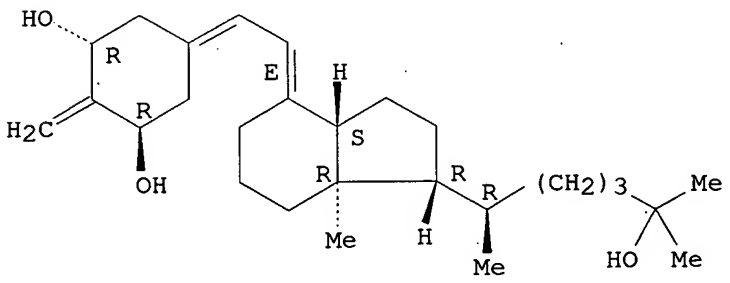
DOCUMENT NUMBER: 139:271426
TITLE: 2-Methylene-19-nor-(20S)-1,25-dihydroxyvitamin D3 potently stimulates gene-specific DNA binding of vitamin D receptor in osteoblasts
AUTHOR(S): Yamamoto, Hironori; Shevde, Nirupama K.; Warrier, Anjali; Plum, Lori A.; DeLuca, Hector F.; Pike, J. Wesley
CORPORATE SOURCE: Department of Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706, USA
SOURCE: Journal of Biological Chemistry (2003), 278(34), 31756-31765
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

IT 213319-29-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(2-methylene-19-nor-(20S)-1,25-dihydroxyvitamin D3 potently stimulates gene-specific DNA binding of vitamin D receptor in osteoblasts in relation to underlying mol. mechanism)
RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB 2-Methylene-19-nor-(20S)-1,25-dihydroxyvitamin D3 (2MD) is a highly potent analog of 1,25-dihydroxyvitamin D3 (1,25(OH)2D3) whose actions are mediated through the vitamin D receptor (VDR). The authors have replicated this increased potency of 2MD in vitro using osteoblastic cells and explored its underlying mol. mechanism. 2MD stimulates the expression of several vitamin D-sensitive genes including 25-hydroxyvitamin D3-24 hydroxylase (Cyp24), osteopontin and receptor activator of NFκB ligand and suppresses osteoprotegerin at concns. two logs lower than that for 1,25(OH)2D3. 2MD is also more potent in stimulating transfected chimeric reporter genes under either Cyp24 or the osteocalcin promoter control. Enhanced potency is retained regardless of medium serum content. Interestingly, the uptake of both 1,25(OH)2D3 and 2MD into cells is similar, as is their rapid association with the VDR. This indicates that comparable levels of occupied VDR do not elicit equivalent levels of transactivation. Using chromatin immunopptn. (ChIP), however, the authors observed a strong correlation between DNA-bound receptor and the level of induced transcription suggesting a 2MD-induced increase in affinity of the VDR for DNA. Addnl. studies using a mammalian two-hybrid system and ChIP

indicate that 2MD is also more potent in promoting interaction with RXR and the coactivators SRC-1 and DRIP205. Finally, protease digestion studies revealed a unique VDR conformation in the presence of 2MD. These studies suggest that the mol. mechanism of 2MD potency is due to its ability to promote enhanced levels of specific DNA binding by the VDR and could suggest possible explanations for the tissue- and gene-selective actions of 2MD.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 24 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:387626 CAPLUS
DOCUMENT NUMBER: 136:401925
TITLE: Preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compounds as antiosteoporotics and antitumor agents
INVENTOR(S): Deluca, Hector F.; Sicinski, Rafal R.
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: U.S., 22 pp., Cont.-in-part of U.S. Ser. No. 370,966, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6392071	B1	20020521	US 2000-540686	20000331
US 5843928	A	19981201	US 1997-819693	19970317
US 5936133	A	19990810	US 1998-151113	19980910
CA 2404548	A1	20011011	CA 2001-2404548	20010329
WO 2001074766	A1	20011011	WO 2001-US10317	20010329
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EP 1268416	A1	20030102	EP 2001-920897	20010329
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JP 2003529581	T	20031007	JP 2001-572461	20010329
NZ 522160	A	20041126	NZ 2001-522160	20010329
US 2002087015	A1	20020704	US 2001-1711	20011031
US 6537981	B2	20030325		
US 2003181427	A1	20030925	US 2003-352745	20030128
US 6696431	B2	20040224		
US 2004167104	A1	20040826	US 2004-780103	20040217
US 7094774	B2	20060822		
JP 2006117680	A	20060511	JP 2005-319365	20051102

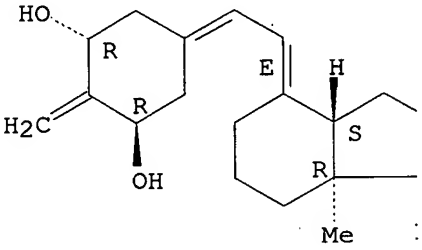
PRIORITY APPLN. INFO.:

US 1997-819693	A3 19970317
US 1998-151113	A1 19980910
US 1999-370966	B2 19990810
JP 1998-540501	A3 19980211

QAZI

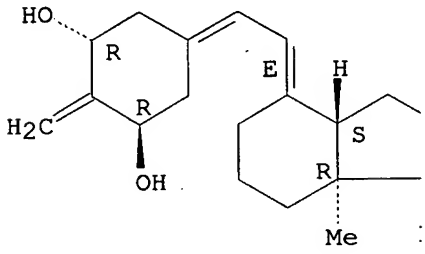
OTHER SOURCE(S): M
IT 213250-70-5P 213319-2
RL: PAC (Pharmacologi
(Therapeutic use); BI
(Uses)
(preparation of 26
compds. as antiost
RN 213250-70-5 CAPLUS
CN 19-Nor-9,10-secochole
(1α,3β,7E,20S)- (9CI)

Absolute stereochemistry.
Double bond geometry as sh



RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secochole
(1α,3β,7E)- (9CI) (C

Absolute stereochemistry.
Double bond geometry as sh



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* STRUCTURE DIAGRAM TOO LA

AB Novel vitamin D relat
derivs. of formula I

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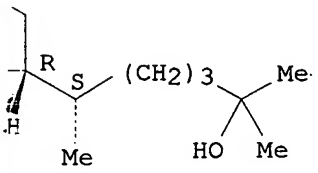
cal activity); SPN (Synthetic preparation); THU
OL (Biological study); PREP (Preparation); USES

,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D
eoporotics and antitumor agents)

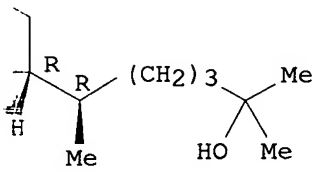
sta-5,7-diene-1,3,25-triol, 2-methylene-,
(CA INDEX NAME)

own.



sta-5,7-diene-1,3,25-triol, 2-methylene-,
A INDEX NAME)

own.



RGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

ed compds., namely, 2-alkylidene-19-nor-vitamin D
[Y1, Y2 = H, protecting group; R6, R8 = alkyl,

US 2000-540686	A	20000331
WO 2001-US10317	W	20010329
US 2001-1711	A3	20011031
US 2003-352745	A3	20030128

ARPAT 136:401925
9-0P
cal activity); SPN (Synthetic preparation); THU

hydroxyalkyl, fluoroalkyl, etc., or when taken together represent the group -(CH2)x- where x is an integer from 2 to 5; R = any of the typical side chains known for vitamin D type compds.] are prepared These 2-substituted compds. are characterized by low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. Thus, 20(S)-1α,25-dihydroxy-2-methylene-26,27-dihomo-19-nor-vitamin D3 (II) was prepared via a multistep synthetic sequence starting from 20(S)-25-hydroxy Grundmann's ketone analog III and phosphine oxide IV. The intestinal calcium transport and serum calcium (bone calcium mobilization) activities in vitamin D-deficient rats on a low calcium diet responding to chronic doses of II at 15 pmol/day/7 days were 4.0 ± 0.4 S/M and 5.3 ± 0.1 S/M resp. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

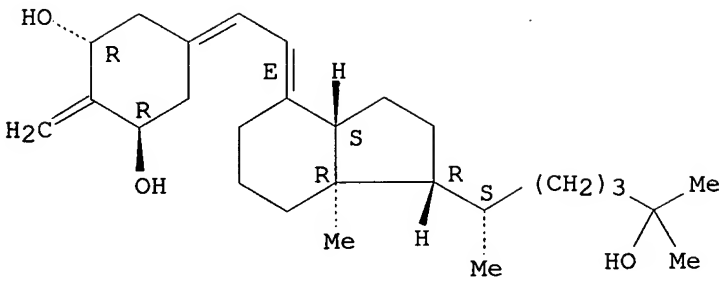
L10 ANSWER 25 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:332679 CAPLUS
DOCUMENT NUMBER: 136:335278
TITLE: 1α-Hydroxy-2-methylene-19-nor-homopregnacalciferol and its therapeutic uses
INVENTOR(S): DeLuca, Hector F.; Sicinski, Rafal R.; Gowlugari, Sumithra; Plum, Lori A.; Clagett-Dame, Margaret
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U. S. Ser. No. 657,828.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002052350	A1	20020502	US 2001-878438	20010611
US 6440953	B2	20020827		
PT 1315504	T	20041231	PT 2001-942154	20010611
ES 2227215	T3	20050401	ES 2001-1942154	20010611
US 2002183289	A1	20021205	US 2002-165123	20020607
US 6579861	B2	20030617		
PRIORITY APPLN. INFO.:			US 2000-657828 A2	20000908
			US 2001-878438 A3	20010611

IT 213250-70-5
RL: PAC (Pharmacological activity); BIOL (Biological study)
(hydroxymethylenenorhomopregnacalciferol and therapeutic use)
RN 213250-70-5 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

QAZI



AB The invention discloses 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol and its pharmaceutical uses. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

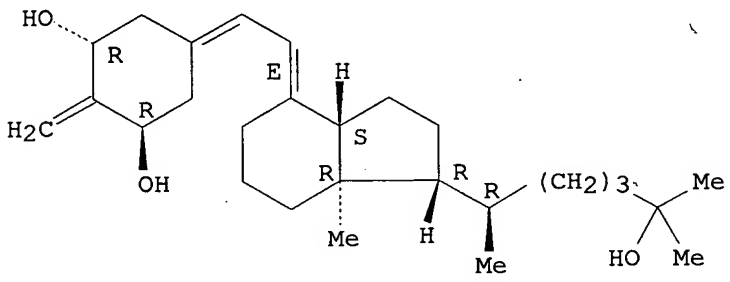
L10 ANSWER 26 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:71881 CAPLUS
DOCUMENT NUMBER: 136:112696
TITLE: Use of 2-methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D3 to increase bone strength and for the treatment of skin disease, cancer, and bone disease
INVENTOR(S): Deluca, Hector F.; Smith, Connie M.
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002005823	A2	20020124	WO 2001-US21706	20010710
WO 2002005823	A3	20020523		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2416194	A1	20020124	CA 2001-2416194	20010710
AU 2001078888	A5	20020130	AU 2001-78888	20010710
EP 1301189	A2	20030416	EP 2001-957115	20010710
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012454	A	20030729	BR 2001-12454	20010710

JP 2004505022	T	20040219	JP 2002-511755		20010710
NZ 537036	A	20060728	NZ 2001-537036		20010710
US 2004068129	A1	20040408	US 2003-673629		20030929
US 7115594	B2	20061003			
HK 1060304	A1	20060421	HK 2004-103322		20040512
US 2006135492	A1	20060622	US 2006-350554		20060209
US 2006135493	A1	20060622	US 2006-350555		20060209
PRIORITY APPLN. INFO.:			US 2000-616164	A	20000714
			WO 2001-US21706	W	20010710
			US 2003-673629	A3	20030929

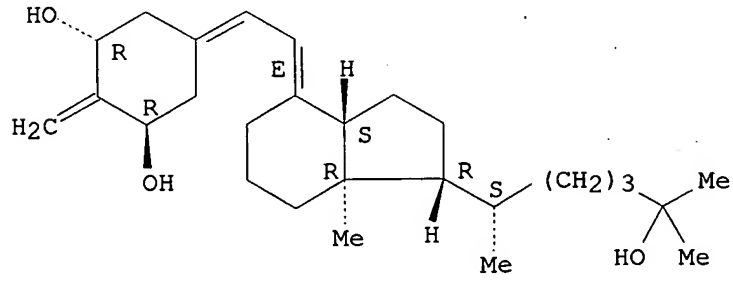
IT 213319-29-0
RL: PAC (Pharmacological activity); BIOL (Biological study)
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT 213250-70-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methylenenordihydroxyvitamin D3 to increase bone strength and for treatment of skin disease, cancer, and bone disease)
RN 213250-70-5 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB The invention provides pharmaceutical uses for 2-methylene-19-nor-20(S)-

1α,25-dihydroxyvitamin D3. This compound is characterized by high bone calcium mobilization activity demonstrating preferential activity on bone. This results in a novel therapeutic agent for the treatment of diseases where bone formation is desired, particularly osteoporosis. This compound also exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte, thus evidencing use as an anticancer agent and for the treatment of skin diseases such as psoriasis. This compound also increases both breaking strength and crushing strength of bones evidencing use in conjunction with bone replacement surgery such as hip and knee replacements.

L10 ANSWER 27 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:830900 CAPLUS
DOCUMENT NUMBER: 135:358086
TITLE: Preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compounds
INVENTOR(S): Deluca, Hector F.; Sicinski, Rafal R.
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: U.S., 33 pp., Cont.-in-part of U.S. Ser. No. 454,013.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6316642	B1	20011113	US 2000-541470	20000331
US 5945410	A	19990831	US 1997-819694	19970317
US 6127559	A	20001003	US 1998-135463	19980817
US 6277837	B1	20010821	US 1999-454013	19991203
CA 2403232	A1	20011011	CA 2001-2403232	20010329
WO 2001074765	A1	20011011	WO 2001-US10094	20010329
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1268415	A1	20030102	EP 2001-920863	20010329
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004500414	T	20040108	JP 2001-572460	20010329
NZ 521236	A	20051028	NZ 2001-521236	20010329
US 2002123638	A1	20020905	US 2001-999299	20011031
US 6544969	B2	20030408		
US 2003073857	A1	20030417	US 2002-246968	20020919
US 6667298	B2	20031223		
US 2004072804	A1	20040415	US 2003-673618	20030929
US 6939868	B2	20050906		
US 2004082802	A1	20040429	US 2003-683330	20031010
US 7112579	B2	20060926		
JP 2006096759	A	20060413	JP 2005-319359	20051102
PRIORITY APPLN. INFO.:			US 1997-819694	A2 19970317
			US 1998-135463	A3 19980817

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US	1999-454013	A2 19991203
JP	1998-540500	A3 19980211
US	2000-541470	A 20000331
WO	2001-US10094	W 20010329
US	2001-45941	B3 20011019
US	2001-999299	A3 20011031
US	2002-246968	A3 20020919

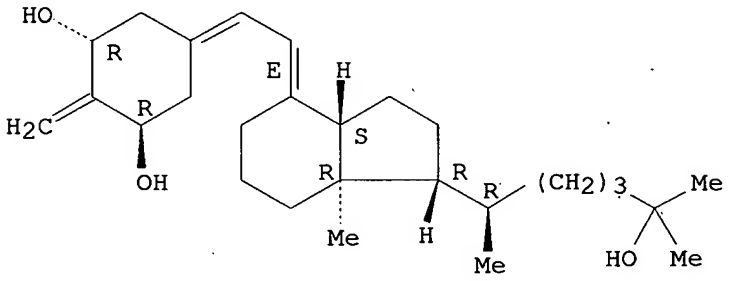
OTHER SOURCE(S): MARPAT 135:358086

IT 213319-29-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 26,27-homologated-20-epi-2-alkyl-19-norvitamin D compds. with high intestinal calcium transport activity)

RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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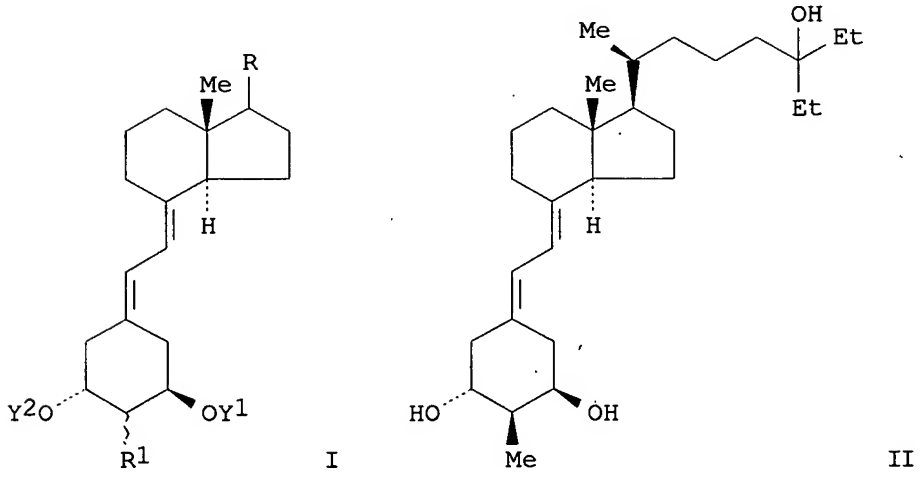

AB 2-Alkyl-19-nor-vitamin D derivs. of formula I [Y1, Y2 = H, protecting

group; R = typical side chains known for vitamin D type compds.; R1 = alkyl, hydroxyalkyl, fluoroalkyl] are prepared These 2-substituted compds., especially the 2α-Me and the 2α-methyl-20S derivs., are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anticancer agents and for the treatment of diseases such as psoriasis. Thus, II was prepared and showed preferential activity on bone in biol. activity tests.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 28 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:747743 CAPLUS
DOCUMENT NUMBER: 135:288953
TITLE: Preparation of 2-alkylidene-19-nor-vitamin D compounds as antiosteoporotics and antitumor agents
INVENTOR(S): Deluca, Hector F.; Sicinski, Rafal R.
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001074766	A1	20011011	WO 2001-US10317	20010329
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6392071	B1	20020521	US 2000-540686	20000331
CA 2404548	A1	20011011	CA 2001-2404548	20010329
EP 1268416	A1	20030102	EP 2001-920897	20010329
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003529581	T	20031007	JP 2001-572461	20010329
NZ 522160	A	20041126	NZ 2001-522160	20010329
PRIORITY APPLN. INFO.:			US 2000-540686	A 20000331
			US 1997-819693	A3 19970317
			US 1998-151113	A1 19980910
			US 1999-370966	B2 19990810
			WO 2001-US10317	W 20010329

OTHER SOURCE(S): MARPAT 135:288953
IT 213319-29-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

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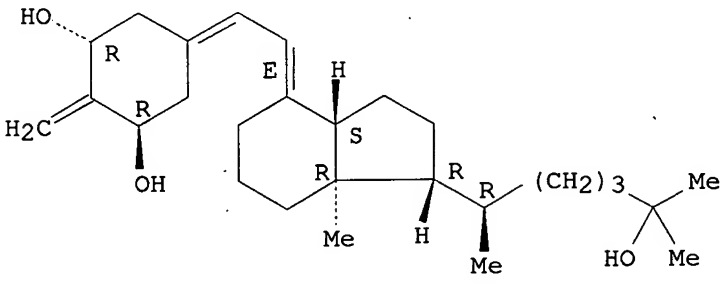
(preparation of 2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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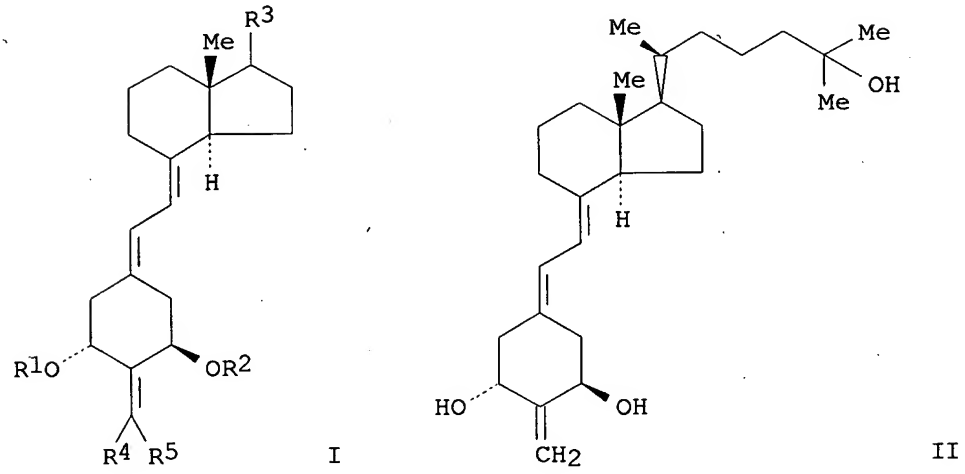


I II

AB Novel vitamin D related compds., namely, 2-alkylidene-19-nor-vitamin D derivs. of formula I [R1, R2 = H, protecting group; R3 = typical side chains known for vitamin D type compds.; R4, R5 = H, alkyl, hydroxyalkyl, fluoroalkyl, etc.; R4R5 = cycloalkylidene] are prepared These 2-substituted compds. are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anticancer agents and for the treatment of diseases such as psoriasis. Thus, II is prepared and is found to be extremely potent

in inducing differentiation of HL-60 cells.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 29 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:747742 CAPLUS
DOCUMENT NUMBER: 135:304063
TITLE: Preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compounds
INVENTOR(S): Deluca, Hector F.; Sicinski, Rafal R.
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

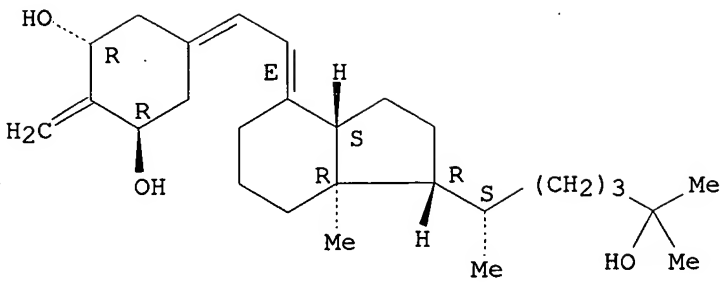
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001074765	A1	20011011	WO 2001-US10094	20010329
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6316642	B1	20011113	US 2000-541470	20000331
CA 2403232	A1	20011011	CA 2001-2403232	20010329
EP 1268415	A1	20030102	EP 2001-920863	20010329
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004500414	T	20040108	JP 2001-572460	20010329
NZ 521236	A	20051028	NZ 2001-521236	20010329
US 2004072804	A1	20040415	US 2003-673618	20030929
US 6939868	B2	20050906		

PRIORITY APPLN. INFO.:	US 2000-541470	A	20000331
	US 1997-819694	A2	19970317
	US 1998-135463	A3	19980817
	US 1999-454013	A2	19991203
	WO 2001-US10094	W	20010329
	US 2001-45941	B3	20011019

OTHER SOURCE(S): MARPAT 135:304063
IT 213250-70-5P 213319-29-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)
RN 213250-70-5 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

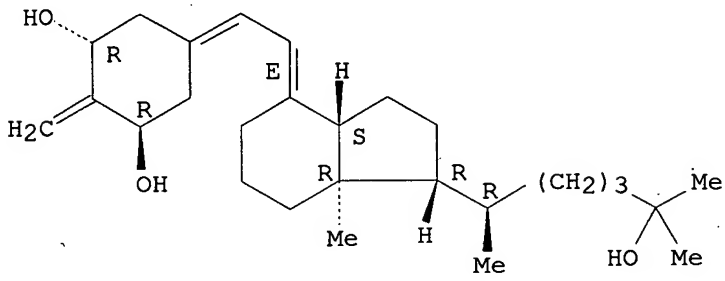
Absolute stereochemistry.
Double bond geometry as shown.

QAZI



RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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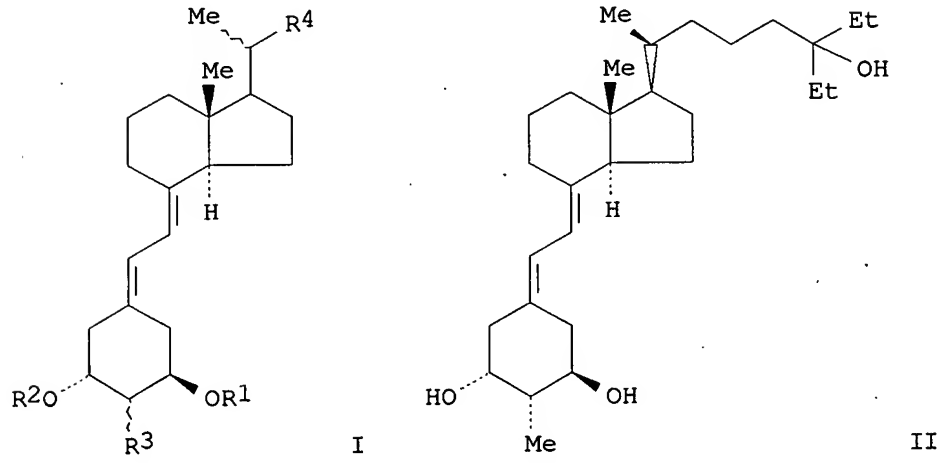

AB 2-Alkyl-19-nor-vitamin D derivs. of formula I [R1, R2 = H, protecting group; R3 = alkyl, hydroxyalkyl, fluoroalkyl; R4 = H, Me, acyl, OH, any of the typical side chains known for vitamin D type compds., etc.] are prepared

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These compds. are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis. Thus, II is prepared and had a VDR binding ratio of 5.5, and HL-60 differentiation ED50 of 1.1 x 10-10 M.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 30 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:699222 CAPLUS
DOCUMENT NUMBER: 133:267021
TITLE: preparation and therapeutic use of 2-alkyl-19-nor-vitamin D derivatives
INVENTOR(S): Deluca, Hector F.; Sicinski, Rafal R.
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: U.S., 27 pp., Cont.-in-part of U.S. 5,945,410.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6127559	A	20001003	US 1998-135463	19980817
US 5945410	A	19990831	US 1997-819694	19970317
PT 971888	T	20040331	PT 1998-905101	19980211
ES 2206893	T3	20040516	ES 1998-905101	19980211
US 6277837	B1	20010821	US 1999-454013	19991203
US 6316642	B1	20011113	US 2000-541470	20000331
US 6306844	B1	20011023	US 2000-616778	20000714
US 2002151528	A1	20021017	US 2001-45941	20011019
US 2002123638	A1	20020905	US 2001-999299	20011031
US 6544969	B2	20030408		
US 2003073857	A1	20030417	US 2002-246968	20020919
US 6667298	B2	20031223		
US 2004072804	A1	20040415	US 2003-673618	20030929
US 6939868	B2	20050906		
US 2004082802	A1	20040429	US 2003-683330	20031010
US 7112579	B2	20060926		
US 2006003973	A1	20060105	US 2005-216951	20050831
JP 2006096759	A	20060413	JP 2005-319359	20051102

PRIORITY APPLN. INFO.:

US 1997-819694	A2	19970317
JP 1998-540500	A3	19980211
US 1998-135463	A3	19980817
US 1999-454013	A2	19991203
US 2000-541470	A3	20000331
US 2000-616778	A3	20000714
JP 2001-83085	A	20010322
US 2001-45941	B3	20011019
US 2001-999299	A3	20011031
US 2002-246968	A3	20020919
US 2003-673618	A3	20030929

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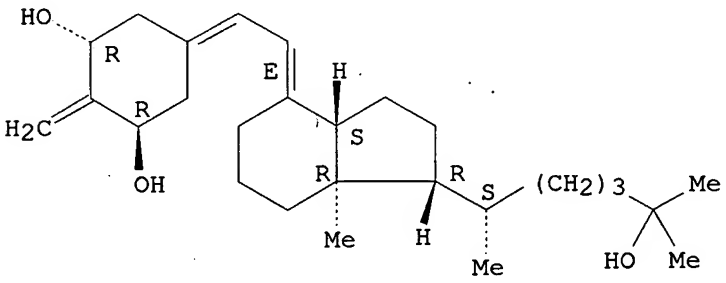
OTHER SOURCE(S): MARPAT 133:267021

IT 213250-70-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation and therapeutic use of 2-alkyl-19-nor-vitamin D analog)

RN 213250-70-5 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

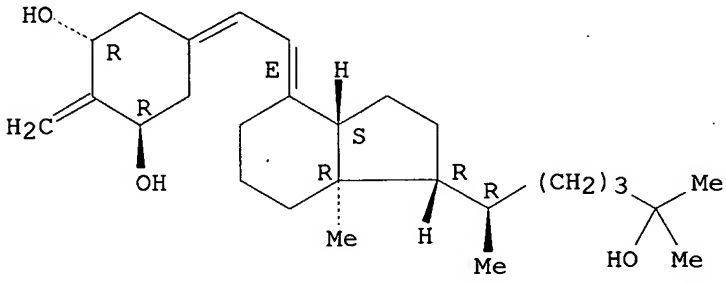


IT 213319-29-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and therapeutic use of 2-alkyl-19-nor-vitamin D analog)

RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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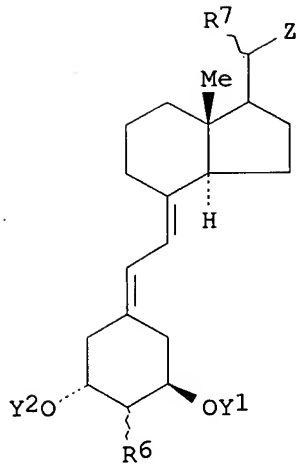

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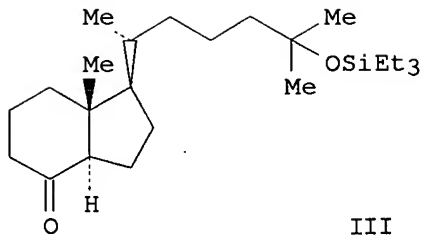

III

AB This invention discloses a novel class of vitamin D related compds., namely, the 2-alkyl-19-nor-vitamin D derivs. (I) (Y1,Y2 = H, hydroxy-protecting group; R6 = alkyl, hydroxyalkyl, fluoroalkyl; R7 = α or β-Me; Z = Y, -OY, -CH2OY, -C.tplbond.CY, -CH=CHY (Y = H, Me, -(CH2)m-C(R1R2)-(CH2)n-C(R3R4R5); where m and n, independently integers from 0-5; R1 = H, OH, protected hydroxy, F, CF3, alkyl etc., R2, R3, R4 = D, deuteroalkyl, H, F, CF3, alkyl etc., R1+R2 = O, =C(R2R3) etc., R5 = H, OH, protected hydroxy, alkyl, and wherein any of the CH-groups at position 20,22, or 23 in the side chain may be replaced by a N atom or where any of the groups -CH(Me)-, -CH(R3)-, or -CH(R2)- at positions 20, 22, and 23, resp., may be replaced by an oxygen or sulfur atom)), were prepared Thus, I (Y1,Y2 = H; R6,R7 = α-Me; Z = (CH2)3C(Me)2OH) (II) was prepared starting from Me quinicate and followed by Wittig-Horner coupling with Grundman's ketone (III). The 2-substituted compds., especially the 2α-Me and the 2α-methyl-20S derivs., are characterized by relatively low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. I also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 31 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:505692 CAPLUS
DOCUMENT NUMBER: 131:144749
TITLE: Preparation of 14-epi-19-nor-vitamin D compounds with cell differentiation activity
INVENTOR(S): Paaren, Herbert E.
PATENT ASSIGNEE(S): Tetrionics, Inc., USA
SOURCE: U.S., 14 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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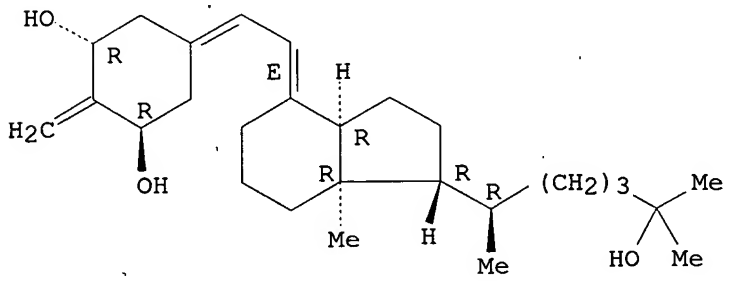
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 5936105	A	19990810	US 1998-96330		19980611
PRIORITY APPLN. INFO.:			US 1997-53088P	P	19970613

IT 235108-14-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 14-epi-19-nor-vitamin D compds. with cell differentiation activity)
RN 235108-14-2 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,14β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB 14-Epi-19-nor-vitamin D analog compds. are prepared with high cell differentiation and antiproliferative activity and low calcemic activity. More particularly, examples of such compds. include 14-epi-19-nor-1α,25-dihydroxyvitamin D3, 14-epi-20-epi-19-nor-1α,25-dihydroxyvitamin D3 (I), 14-epi-20-epi-19-nor-1α-hydroxyvitamin D3, 14-epi-19-nor-1α,25-dihydroxyvitamin D2, 14-epi-19-nor-24-homo-1α,25-dihydroxyvitamin D3, 14-epi-19-nor-20(S)-hydroxymethyl-1α-hydroxypregnacalciferol, and 14-epi-19-nor-20(R)-hydroxymethyl-1α-hydroxypregnacalciferol. Thus, I was prepared and showed an EC50 of 0.66 nM to inhibit proliferation of HL-60 cells.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 32 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:672847 CAPLUS
DOCUMENT NUMBER: 130:52625
TITLE: New 1α,25-Dihydroxy-19-norvitamin D3 Compounds of High Biological Activity: Synthesis and Biological Evaluation of 2-Hydroxymethyl, 2-Methyl, and 2-Methylene Analogs
AUTHOR(S): Sicinski, Rafal R.; Prahl, Jean M.; Smith, Connie M.; DeLuca, Hector F.
CORPORATE SOURCE: Department of Biochemistry College of Agricultural and Life Sciences, University of Wisconsin-Madison, Madison, WI, 53706, USA
SOURCE: Journal of Medicinal Chemistry (1998), 41(23), 4662-4674
CODEN: JMCMAR; ISSN: 0022-2623

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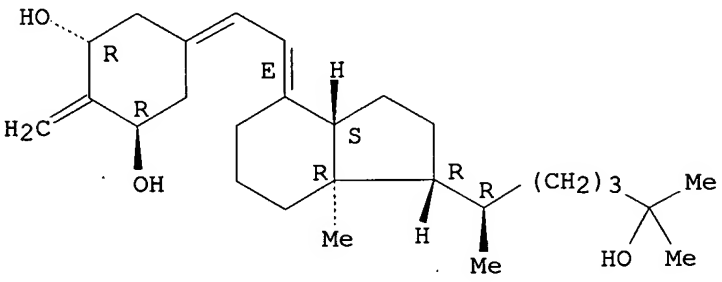
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 213319-29-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and biol. evaluation of 2-hydroxymethyl, 2-Me, and 2-methylene 1α,25-dihydroxy-19-norvitamin D3 analogs)
RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB New highly active isomers of the natural hormone 1α,25-dihydroxyvitamin D3 possessing an exomethylene group at the 2-position were prepared in a convergent manner, starting with (-)-quinic acid and the corresponding (20R)- and (20S)-25-hydroxy Grundmann ketones. These 2-methylene-19-norvitamins were efficiently converted to the 2-Me and 2-hydroxymethyl derivs., some of which exhibited pronounced in vivo biol. activity. Configurations of the A-ring substituents were determined by 1H NOE difference spectroscopy as well as by spin decoupling expts. It was established that the bulky Me and hydroxymethyl substituents at C-2, due to their large conformational free energies, occupy mainly equatorial positions. Addnl., hydroxylation of the C(10)-C(19) double bond in 1α,25-(OH)2D3 was performed, resulting in 1α,19,25-trihydroxy-10,19-dihydrovitamin D3 derivs. in which the hydroxymethyl substituent at C-10, for steric reasons, is forced to occupy an axial position. In consequence, the vitamin D3 analogs were synthesized in which the 1α-hydroxy group, required for biol. activity, is almost exclusively axially or equatorially oriented because of stabilization of the single A-ring chair conformations. The relative ability of the synthesized analogs to bind the porcine intestinal vitamin D receptor was assessed and compared with that of the natural hormone. It was established that vitamins possessing the axial orientation of the 1α-hydroxy substituent exhibit a significantly increased receptor binding affinity. Compds. with a 2-methylene substituent showed selective calcemic activity profiles, being extremely effective on bone calcium mobilization. 2α-Methyl-substituted vitamins proved to be much more active in vivo than the corresponding epimers with 2β-configuration. All of the 2-substituted vitamins exhibited pronounced HL-60 differentiating activity, those 2α-substituted in the 20S-series being especially potent. The present studies imply that the axial orientation of the 1α-hydroxy group is necessary for biol. activity of vitamin D

compds.
REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 33 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:635741 CAPLUS
DOCUMENT NUMBER: 129:245333
TITLE: Preparation of 2-alkylidene-19-nor-vitamin D compounds
INVENTOR(S): Deluca, Hector F.; Sicinski, Rafal R.
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9841501	A1	19980924	WO 1998-US2976	19980211
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GW, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5843928	A	19981201	US 1997-819693	19970317
CA 2283829	A1	19980924	CA 1998-2283829	19980211
CA 2283829	C	20060711		
AU 9862801	A	19981012	AU 1998-62801	19980211
AU 714253	B2	19991223		
EP 970047	A1	20000112	EP 1998-905102	19980211
EP 970047	B1	20020911		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 337503	A	20000929	NZ 1998-337503	19980211
JP 2001504135	T	20010327	JP 1998-540501	19980211
JP 3786713	B2	20060614		
AT 223890	T	20020915	AT 1998-905102	19980211
ES 2179451	T3	20030116	ES 1998-905102	19980211
PT 970047	T	20030131	PT 1998-905102	19980211
NO 9904398	A	19990910	NO 1999-4398	19990910
NO 322535	B1	20061023		
JP 2006117680	A	20060511	JP 2005-319365	20051102
			US 1997-819693 A	19970317
PRIORITY APPLN. INFO.:			JP 1998-540501 A3	19980211
			WO 1998-US2976 W	19980211

OTHER SOURCE(S): MARPAT 129:245333
IT 213250-70-5P
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-alkylidenenor-vitamin D compds.)
RN 213250-70-5 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,

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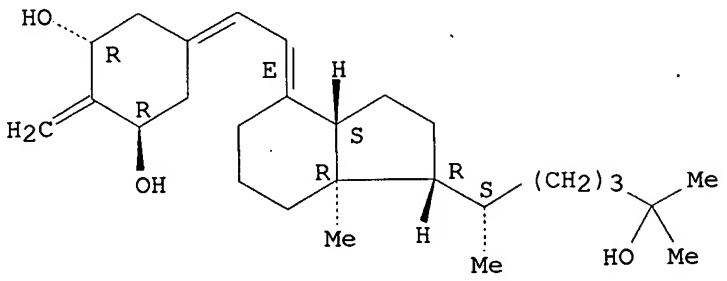
(1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; Y1, Y2 = H, protecting group; R6, R8 = H, alkyl, hydroxyalkyl, fluoroalkyl, or R6R8 = (CH2)x; x = 2-5 integer; R = any of the typical side chains known for vitamin D type compds., e.g. Q] are prepared Thus, 1α,25-dihydroxy-2-methylene-19-norvitamin D3 (II) was prepared in 11 steps from (-)-quinic acid via tert-butyldimethylsilyl protection of the OH groups at the 3 and 5 positions, converting to protected quinic acid Me ester, oxidation of the 4-OH, methylenation using methyltriphenylphosphonium bromide, hydride reduction, NaIO4 oxidation, condensation of 3,5-bis(tert-butyldimethylsilyloxy)-4-methylenecyclohexanone with Me3SiCH2-COOMe, DIBAL reduction, reaction with Ph2PH, H2O2 oxidation, condensation with perhydroindanone III in the presence of BuLi, and deprotection. These 2-substituted compds. are characterized by low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. The intestinal calcium transport and serum calcium (bone calcium mobilization) activities in rats responding to chronic doses of II at 130 pmol/day/7 days were 5.3±0.4 S/M and 9.9±0.2 mg/100 Ml, resp., vs. 6.2±0.4 S/M and 7.2±0.5 mg/100 mL, resp., for 1,25-(OH)2D3. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 34 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:635740 CAPLUS
DOCUMENT NUMBER: 129:245332
TITLE: Preparation of 2-alkyl-19-nor-vitamin D compounds and their biological activities
INVENTOR(S): Deluca, Hector F.; Sicinski, Rafal R.
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: PCT Int. Appl., 55 pp.

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CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9841500	A1	19980924	WO 1998-US2975	19980211
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GW, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5945410	A	19990831	US 1997-819694	19970317
CA 2272745	A1	19980924	CA 1998-2272745	19980211
CA 2272745	C	20051206		
AU 9862800	A	19981012	AU 1998-62800	19980211
AU 714390	B2	19991223		
EP 971888	A1	20000119	EP 1998-905101	19980211
EP 971888	B1	20031029		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9808010	A	20000308	BR 1998-8010	19980211
NZ 337262	A	20000929	NZ 1998-337262	19980211
JP 2000513010	T	20001003	JP 1998-540500	19980211
JP 3786712	B2	20060614		
AT 253046	T	20031115	AT 1998-905101	19980211
PT 971888	T	20040331	PT 1998-905101	19980211
ES 2206893	T3	20040516	ES 1998-905101	19980211
NO 9904489	A	19990916	NO 1999-4489	19990916
NO 321925	B1	20060724		
US 2004072804	A1	20040415	US 2003-673618	20030929
US 6939868	B2	20050906		
JP 2006096759	A	20060413	JP 2005-319359	20051102

PRIORITY APPLN. INFO.:

US 1997-819694	A	19970317
JP 1998-540500	A3	19980211
WO 1998-US2975	W	19980211
US 2001-45941	B3	20011019

OTHER SOURCE(S): MARPAT 129:245332

IT 213250-70-5P 213319-29-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)

RN 213250-70-5 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

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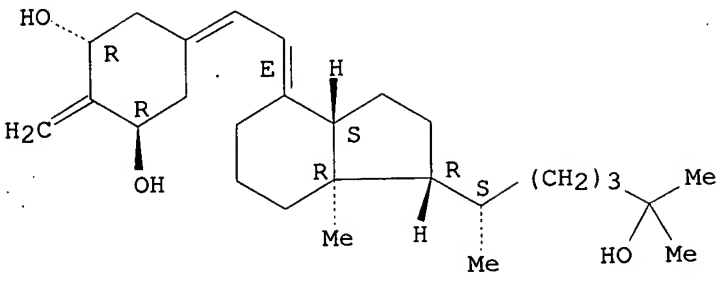
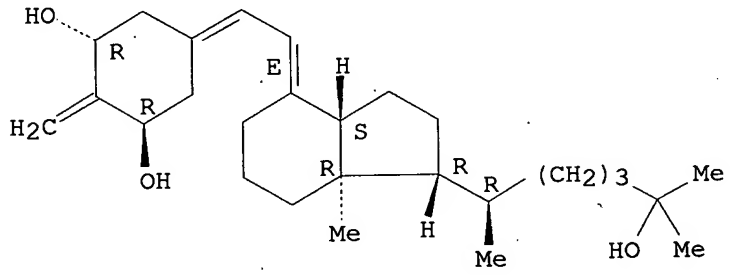


RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1α,3β,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; Y1, Y2 = H, protecting group; R6 = alkyl, hydroxyalkyl, fluoroalkyl, etc.; R = any of the typical side chains known for vitamin D type compds., e.g. Q] are prepared Thus, 1α,25-dihydroxy-2α- and 1α,25-dihydroxy-2β-methyl-19-norvitamin D3 (II) were prepared in 11 steps from (-)-quinic acid via tert-butyldimethylsilyl protection of the OH groups at positions 3 and 5, converting to protected quinic acid Me ester, oxidation of the 4-OH, methylenation using methyltriphenylphosphonium bromide, hydride reduction, NaIO4 oxidation, condensation of the resulting 3,5-bis(tert-butyldimethylsilyloxy)-4-methylcyclohexanone with Me3SiCH2COOMe, DIBAL reduction, reaction with Ph2PH, oxidation, condensation with perhydroindanone III in the presence of BuLi, and deprotection. These 2-substituted compds. are characterized by low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. The intestinal calcium transport and serum calcium (bone calcium mobilization) activities in rats responding to chronic doses of II (both epimers) at 130 pmol/day/7 days

QAZI

were 5.0±0.3 S/M and 6.1±0.1 mg/100 mL, resp., vs. 6.2±0.4 S/M and 7.2±0.5 mg/100 mL, resp., for 1,25-(OH)2D3. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> S L10 AND AND dElUCA
MISSING TERM 'AND AND'
The search profile that was entered contains a logical operator followed immediately by another operator.

=> S L10 AND DELUCA/AU
0 DELUCA/AU
L11 0 L10 AND DELUCA/AU

=> S L10 AND DELUCA
44 DELUCA
L12 0 L10 AND DELUCA

=> D HIS

(FILE 'HOME' ENTERED AT 13:30:52 ON 19 JAN 2007)

FILE 'REGISTRY' ENTERED AT 13:31:08 ON 19 JAN 2007
L1 1 S 235108-14-2/RN
L2 1 S 213319-29-0/RN
L3 0 S 2133250-70-5/RN
L4 1 S 213250-70-5/RN

FILE 'CAPLUS' ENTERED AT 13:33:54 ON 19 JAN 2007
L5 0 S L1 AND L2 AND L4
L6 1 S L1
L7 29 S L2
L8 48 S L4
L9 27 S L7 AND L8
L10 34 S L1 OR L2 OR L4 AND CANCER
L11 0 S L10 AND DELUCA/AU
L12 0 S L10 AND DELUCA

=> LOGOFF
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:h

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	189.91	198.22

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-26.52	-26.52

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STN INTERNATIONAL SESSION SUSPENDED AT 13:39:53 ON 19 JAN 2007

Connecting via Winsock to STN

QAZI

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LOGINID:ssspta1202sxq

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	189.91	198.22

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CA SUBSCRIBER PRICE	-26.52	-26.52

=> LOGOFF
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:h

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	190.38	198.69

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-26.52	-26.52

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STN INTERNATIONAL SESSION SUSPENDED AT 13:41:31 ON 19 JAN 2007